REMARKS

Reconsideration and allowance of the above-identified application are respectfully requested.

Claims 1, 2, 5-7, and 9-12 are currently pending, wherein claim 1 is independent. Claims 3, 4, 8, and 13-68 have been canceled, without prejudice or disclaimer. Applicants reserve the right to file one or more divisional applications directed to the non-elected inventions. Claims 1, 5, 6, and 12 have been amended. Claim 69 and 70 have been added. No new matter has been introduced by way of these amendments or new claims.

Applicants note with appreciation the acceptance by the Patent Office of the drawings filed on September 10, 2003. However, Applicants respectfully note that formal drawings were filed on April 8, 2004, in response to a Notice to File Missing Parts of Nonprovisional Application. In the next communication from the Patent Office, Applicants request that the Patent Office provide acknowledgment of the acceptance of the formal drawings filed on April 8, 2004.

Applicants further note with appreciation the acknowledgment by the Patent Office of the references submitted in the information disclosure statement filed November 5, 2005, and June 23, 2005.

In the second section of the Office Action, claims 1, 2, 5-7, and 9-12 are rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. These rejections are respectfully traversed.

With regard to independent claim 1, the Patent Office alleges that it is apparently unclear "whether the immunosensor system requires an immobilized antibody, a target analyte and a labeled antibody in the form of a sandwich, or whether the immunosensor merely requires a sensor that is capable of generating a signal based on a sandwich." [Office Action, page 2]

According to M.P.E.P. § 2173.02,

> [t]he examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph, is whether the claim meets the threshold requirements of clarity and precision, *not* whether more suitable language or modes of expression are available. . . . Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire. Examiners are encouraged to suggest claim language to applicants to improve the clarity or precision of the language used, **but should not reject claims or insist on their own preferences if other modes of expression selected by applicants satisfy the statutory requirement**. [M.P.E.P. § 2173.02 (emphasis added)]

Given the "latitude in the manner of expression and the aptness of terms" afforded to the Applicants, it is respectfully submitted that claim 1 is clear and precise and fully complies with the requirements of 35 U.S.C. § 112, second paragraph.

More particularly, it is respectfully submitted that independent claim 1 clearly recites that the signal generated by the first immunosensor is "based on the formation of a sandwich between an immobilized antibody, a target analyte and a labeled antibody." As taught by the present application,

> [i]deally, the signal from an immunosensor (IS) is derived solely from the formation of a sandwich between an immobilized antibody (the analyte) and a second antibody that is labeled, wherein the label (e.g., an enzyme) reacts with a substrate to form a detectable product (1).
> (1) Surface-Ab1~analyte~Ab2-enzyme enzyme + S → P
> [present application, paragraph 0081, page 18]

Accordingly, it is respectfully submitted that with regard to the signal generated by the first immunosensor, the plain language of claim 1 is clear and precise and recites what is "required" by the immunosensor system recited in that claim, in full and complete compliance with the mandates of 35 U.S.C. § 112, second paragraph.

Additionally, it is apparently unclear to the Patent Office "whether the immobilized antibody of line 4 [of claim 1] is the same immobilized antibody of line 10 [of claim 1]." [Office Action, page 2] According to the present application,

> [t]he immuno-reference sensor is preferably the same in all significant respects (e.g., dimensions, porous screening layer, latex particle coating, and metal electrode composition) as the immunosensor **except** that the capture antibody for the analyte (for instance, cTnI) is replaced by an antibody to a plasma protein that naturally occurs in samples (both normal and pathological) at a high concentration. [present application, paragraph 0084, page 19 (emphasis added)]

In other words, the immobilized antibody recited at line 10 of claim 1 is a different antibody from the immobilized antibody recited at line 4 of claim 1. Given the "latitude in the manner of expression and the aptness of terms" afforded to the Applicants, it is respectfully submitted that claim 1 is clear and precise and fully complies with the requirements of 35 U.S.C. § 112, second paragraph.

However, merely to facilitate prosecution in the present application, Applicants hereby amend claim 1 to recite that the second immunosensor "has an immunocomplex between *another* immobilized antibody . . . ." This grammatical amendment is made merely to clarify the language of independent claim 1, and is not made for any purposes related to patentability. This

amendment does not narrow or otherwise limit the scope of the claim. The amendment is fully supported by the present application, such as, for example, at paragraph 0084, page 19. No new matter has been introduced by way of this amendment.

The Patent Office also alleges that there is insufficient antecedent basis for the phrase "the sample" recited at line 11 of claim 1. Contrary to the assertions of the Patent Office, according to M.P.E.P. § 2173.05(e), "the failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. *Ex parte Porter*, 25 USPQ2d 1144, 1145 (Bd. Pat. App. & Inter. 1992)." Applicants respectfully submit that one of ordinary skill in the art of the present invention can reasonably ascertain the scope of claim 1. It is respectfully submitted that one of ordinary skill in the art of the present invention can readily discern the scope of "the sample," as claim 1 is directed to "[a]n immunosensor system with reduced interference." Consequently, it is respectfully submitted that claim 1 is clear and precise and reasonably apprises a person of ordinary skill in the art of the invention, in complete compliance with the mandates of 35 U.S.C. § 112, second paragraph.

However, merely to facilitate prosecution in the present application, Applicants hereby amend claim 1 to recite "a sample." This grammatical amendment is made merely to clarify the language of independent claim 1, and is not made for any purposes related to patentability. This amendment does not narrow or otherwise limit the scope of the claim. No new matter has been introduced by way of this amendment.

In addition, the Patent Office alleges that "[i]t is vague as to whether the sample is intended to be claimed as part of the immunosensor or whether the sample is merely used with the immunosensor." [Office Action, page 3] The attention of the Patent Office is directed to the present application that teaches that

> [t]he present invention permits rapid in situ determinations of analytes using a cartridge having an array of analyte sensors and means for sequentially presenting a sample and a fluid (amended or not) to the analyte array . . . . The invention provides cartridges and methods of their use for processing liquid samples to determine the presence or amount of an analyte in the sample. The cartridges contain a metering means, which permits an unmetered volume of sample to be introduced, from which a metered amount is processed by the cartridge and its associated reading apparatus. [present application, paragraphs 0050 and 0051, page 10 (emphasis added)]

Once again, given the "latitude in the manner of expression and the aptness of terms" afforded to the Applicants, it is respectfully submitted that claim 1 is clear and precise and fully complies with the requirements of 35 U.S.C. § 112, second paragraph. In particular, it is respectfully submitted that it is clear that the sample can be used with the immunosensor system recited in claim 1.

Additionally, the Patent Office alleges that "[i]t is vague as to how the second immunosensor can generate a signal that is "predictably related" to the degree of non-specific binding on the first immunosensor." According to M.P.E.P. § 2173.01,

> [a] fundamental principal contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose **so long as any special meaning assigned to a term is clearly set forth in the specification** . . . . Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the court in *In re Swinehart*, 439 F.2d 210, 160

> USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought. [M.P.E.P. § 2173.01 (emphasis added)]

Furthermore,

> [t]he meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed . . . . **When the specification states the meaning that a term in the claim is intended to have, the claim is examined using that meaning, in order to achieve a complete exploration of the applicant's invention and its relation to the prior art.** [M.P.E.P. § 2173.05(a) (emphasis added)]

Accordingly, so long as the specification states the meaning that a term in a claim is intended to have, the claim meets the requirements of 35 U.S.C. § 112, second paragraph.

Applicants respectfully note that the specification of the present application clearly discloses the "special meaning" of the term "predictably related," and that the Patent Office is simply ignoring the teachings of the present application with regard to the recitation of such a feature in claim 1. The attention of the Patent Office is directed to paragraphs 0081 – 0084 on pages 18 and 19, and paragraph 0093 on pages 21-22 of the present application. As taught by the present application, "[a] second immunosensor can be placed in the cartridge that acts as an immuno-reference sensor (IRS) and gives the same (or a predictably related) degree of non-specific binding as occurs on the primary immunosensor." [present application, paragraph 0083, page 18] In other words, "[i]t will be recognized that it is not necessary for the immuno-reference sensor to have all the same non-specific properties as the immunosensor, only that it be **consistently proportional** in both the wash and non-specific binding parts of the assay." [present application, paragraph 0093, pages 21-22] Consequently, it is respectfully submitted

that the specification of the present application clearly sets forth the "special meaning" assigned to the term "predictably related," in full and complete compliance with the mandates of 35 U.S.C. § 112, second paragraph.

With regard to the rejection of dependent claim 5, it is allegedly unclear to the Patent Office whether "a sample" recited in line 2 of claim 5 "is intended to be the same sample recited in line 11 of claim 1." [Office Action, page 3] Again, given the "latitude in the manner of expression and the aptness of terms" afforded to the Applicants, it is respectfully submitted that claim 5 is clear and precise and fully complies with the requirements of 35 U.S.C. § 112, second paragraph. However, merely to facilitate prosecution in the present application, Applicants hereby amend claim 5 to recite "the sample." This grammatical amendment is made merely to clarify the language of claim 5, and is not made for any purposes related to patentability. This amendment does not narrow or otherwise limit the scope of the claim. No new matter has been introduced by way of this amendment.

With regard to the rejection of dependent claims 6 and 12, it is also apparently unclear to the Patent Office "whether the blood sample recited in claims 6 and 12 is the same as 'the sample' recited in line 11 of claim 1." [Office Action, page 3] Once more, given the "latitude in the manner of expression and the aptness of terms" afforded to the Applicants, it is respectfully submitted that claims 6 and 12 are clear and precise and fully comply with the requirements of 35 U.S.C. § 112, second paragraph. However, merely to facilitate prosecution in the present application, Applicants hereby amends claims 6 and 12 to recite "the sample." These grammatical amendments are made merely to clarify the language of claims 6 and 12, and are

not made for any purposes related to patentability. These amendments do not narrow or otherwise limit the scope of these claims. In addition, dependent claims 69 and 70 have been added to recite that the samples recited in respective claims 6 and 12 can comprise blood samples. No new matter has been introduced by way of any of these amendments.

Accordingly, as claims 1, 2, 5-7, 9-12, 69 and 70 fully comply with the requirements of 35 U.S.C. § 112, second paragraph, reconsideration and withdrawal of these grounds of rejection are respectfully requested.

In the second section of the Office Action, claims 1, 9, 11 and 12 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Piran et al. (U.S. Patent No. 6,087,088, hereinafter "Piran"). These rejections are respectfully traversed.

According to an exemplary embodiment of the present invention, a sandwich assay is performed at a first immunosensor. A portion of the generated signal arises from non-specific binding of a labeled antibody to the first immunosensor. The desired portion of the signal derives from the correctly-formed sandwich. [*see* present application, Equation 1, paragraph 0081] However, the undesirable non-specific sources of the signal are associated with binding, as illustrated in Equations 2 and 3 of paragraph 0082 of the present application. Such a result is generally associated with the incomplete washing of the sensor prior to a detection step. According to exemplary embodiments, a second immunosensor seeks to enable reliable correction for non-specific binding at the first immunosensor. The second immunosensor comprises a surface that includes an immobilized antibody that is not for binding the analyte, but, rather, is for binding to a different protein found in the sample. That antibody forms a

complex with the protein and provides a surface that gives a similar degree of non-specific binding of the labeled antibody, from Equations 2 and 3, at both the first and second immunosensors. Thus, subtracting the signal at the second immunosensor from the signal at the first immunosensor (as shown in Equation 4 of Paragraph 0083 of the present application) provides the correct signal for the desired sandwich formation. [*see* present application, Equation 1, Paragraph 0081]

As understood by Applicants, Piran is directed to binding assay techniques that improve accuracy and sensitivity via accounting for interfering factors. These techniques rely on use, in a simultaneous incubation, of two or more different labels, some of which are used primarily to detect analyte, and others to detect interfering substances originating in the sample. According to Piran, the mathematical relationships between the labels allow corrections that lead to more accurate and sensitive determination of the presence and concentration of the analyte. [*see* Piran, Abstract]

It is respectfully submitted that Piran does not teach an immunosensor system comprising at least the feature of "a second immunosensor that acts as an immuno-reference sensor and generates a signal that is the same as or predictably related to the degree of non-specific binding which occurs in the region of the first immunosensor, and has an immunocomplex between another immobilized antibody and an endogenous or exogenous protein that is in a sample and that is not the target analyte," as recited in independent claim 1 of the present application.

According to Piran, the second, "reference" antibody is a non-immobilized second labeled antibody that does not bind to the analyte. [*see* Piran, column 4, lines 40-47] The

reference antibody is also labeled with a label that must be different from the label on the antibody intended to bind to the analyte. In complete contrast to exemplary embodiments of the present application, it is respectfully submitted that the teachings of Piran are directed to a wholly different technique of eliminating interferences from an immunoassay. It is respectfully submitted that Piran requires a minimum of at least two labels. [*see* Piran, column 7, line 52]. In complete contrast, the immunosensor system of claim 1 recites one label. Piran teaches a second labeled antibody, and that the second antibody is not immobilized. Such teachings are thoroughly and completely different than the immunosensor system recited in independent claim 1, and, in particular, the feature of the second immunosensor. Furthermore, the second immunosensor recited in independent claim 1 "generates a signal that is the same as or predictably related to the degree of non-specific binding which occurs in the region of the first immunosensor." It is respectfully submitted that **nowhere** does Piran teach such a type of interference. Rather, Piran is directed to the use of at least two different labels, one for the analyte and one for the interferent, e.g., two distinguishable chemiluminescent labels. [*see* Piran, column 7, lines 32-43]

For at least the foregoing reasons, it is respectfully submitted that Piran do not anticipate the subject matter of independent claim 1.

Dependent claims 9, 11, and 12 variously depend from independent claim 1, and are, therefore, patentably distinguishable over Piran for at least those reasons stated above with regard to claim 1.

For at least the foregoing reasons, it is respectfully submitted that Piran does not anticipate the subject matter of claims 1, 9, 11, and 12. Accordingly, reconsideration and withdrawal of these grounds of rejection are respectfully requested.

In the fourth section of the Office Action, claims 1, 2, 5-7, 9, 10, and 12 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ding et al. (U.S. Application Publication No. 2001/0029048, hereinafter "Ding") in light of Lee et al. (U.S. Patent No. 4,722,889, hereinafter "Lee"). These rejections are respectfully traversed.

As understood by Applicants, Ding is directed to the realization that a single electrochemical binding assay device can be used to determine multiple analytes in a single sample by simultaneous amperometric measurements using a plurality of working electrodes. More particularly, Ding is directed to the realization that by establishing different analyte binding sites, i.e., antibodies or antigens on a solid phase at a distinct separate location and locating separate working electrodes within proximity of those separate locations, one can add enzyme labeled antibodies or antigens depending on the assay format, and then quantitate the amount of enzyme reaction product, whether chemically the same or different, generated by simultaneous amperometric measurement with the independent micro electrode for each area. According to Ding, the independent micro electrode for each area is spatially separated from adjacent analyte so that a measurement can be taken before cross-interference due to diffusion of product from adjacent analyte areas. [*see* Ding, Abstract]

As acknowledged by the Patent Office, "Ding et al. does not specifically teach the portion of the first signal arising from non-specific binding of the labeled antibody in the region of the

first immunosensor." [Office Action, page 5] Therefore, it is respectfully submitted that Ding does not teach or suggest at least the feature of "a second immunosensor that acts as an immuno-reference sensor and generates a signal that is the same as or predictably related to the degree of non-specific binding which occurs in the region of the first immunosensor," as recited in independent claim 1 of the present application.

According to the established mandates of the patent laws, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." [M.P.E.P. § 2131] The Patent Office has admitted that Ding does not teach at least one feature recited in claim 1. Therefore, it is respectfully submitted that there can be no anticipation of claim 1 in light of the teachings of Ding.

However, to circumvent such a deficiency in the present rejection, the Patent Office cites to Lee to purportedly supply the missing feature. Such a combination of references is properly addressed under 35 U.S.C. § 103(a), and Applicants will respond to the rejection as such.

As understood by Applicants, Lee is directed to a method and reagent kit means for assay of a selected antigen such as hCG or CEA in an aliquot of body fluid. The method comprises the steps of: constituting the aliquot in a mixture comprising tracer (which may be an enzyme tracer or a radioactive tracer) conjugated with monoclonal antibody, and separate immobilized monoclonal antibody; incubating the mixture to enable separation of a solid phase antigen antibody conjugate in sandwich relation; and measuring the tracer content and corresponding antigen content of the aqueous phase or the solid phase. The antibody (conjugated and/or immobilized) comprises multiple monoclonal antibodies from different cell lines so that the

specificity of the assay is enhanced, and the possibility of unrecognized antigen fragments is reduced. In addition, the incubation can be carried out with a scavenger monoclonal antibody so that, as an example, in the context of hCG assay, the scavenger chosen for beta subunit selectivity but low hCG affinity is present in the reaction to prevent any possible cross reactivity from analogs of homologous reactivity. [*see* Lee, Abstract]

According to established mandates of the patent laws, "[t]o establish a prima facie case of obviousness . . . there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." [M.P.E.P. § 2142] "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." [M.P.E.P. § 2143.01] "The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved." [*In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000)] The showing must be "clear and particular, and it must be supported by **actual evidence**." [*Teleflex, Inc. v. Ficosa North American Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002) (quoting *In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999)) (emphasis added)] It is not sufficient to rely on "common sense and common knowledge," as there must be specific evidence to support the motivation. [*See In re Lee*, 277 F.3d. 1338, 1344-45, 61 U.S.P.Q.2d 1430, 1434-35 (Fed. Cir. 2002)]

It is respectfully submitted that the Patent Office has made absolutely no showing of a motivation to combine based on actual, specific, evidence. With respect to the combination of Ding and Lee, the Patent Office has not even attempted to provide a single piece of evidence – actual, specific, or otherwise – of a motivation to combine the teachings of Lee with Ding. The Patent Office is **completely silent** as to any alleged motivation. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness.

Rather, according to M.P.E.P. § 2142, "[t]o reach a proper determination under 35 U.S.C. 103, . . . impermissible hindsight must be avoided and the legal conclusion [of obviousness] must be reached on the basis of the facts gleaned from the prior art." "The references must be viewed **without** the benefit of impermissible hindsight vision afforded by the claimed invention." [M.P.E.P. § 2141 (emphasis added)] Furthermore, according to M.P.E.P. § 2143.01, "[t]he mere fact that references can be . . . modified does not render the resultant combination obvious unless the prior art also suggests the desirability of [such modification]." [*citing* In re Mills, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990)]

The Patent Office states that "the instant specification teaches that an antibody that binds to plasma proteins is suitable for generating a signal that is the same or related to the degree of non-specific binding in the region of the first immunosensor . . . ." [Office Action, page 5, citing to page 18, paragraph 0085 of the present application] The Patent Office uses the teachings of Applicants' own specification to assert that that "Ding et al. teach an antibody that binds to fibrogen (a plasma protein) and therefore is capable of generating a signal that is the same or

related to the degree of non-specific binding in the first immunosensor region." [Office Action, page 5]

It is respectfully submitted that the Patent Office's reasoning is clearly, utterly, and unequivocally based on improper hindsight reasoning. The Patent Office **admits** that it is using the teachings of Applicants' own specification as a "road map" to support its rejection using Ding. [*see* Office Action, page 5, citing to page 18, paragraph 0085 of the present application] It is difficult to imagine a more clear example of improper hindsight reasoning. It is respectfully submitted that the rejection is clearly and unequivocally founded upon "knowledge gleaned only from applicant's disclosure." [*see* M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight, and is, therefore, improper.

For at least the foregoing reasons, it is respectfully submitted that Ding and Lee, whether considered alone or in combination, do not render the subject matter of independent claim 1 obvious.

Dependent claims 2, 5-7, 9, 10, and 12 (and 69 and 70) variously depend from independent claim 1, and are, therefore, patentably distinguishable over the combination of Ding and Lee for at least those reasons stated above with regard to claim 1.

With regard to the rejection of claims 9 and 12, it is respectfully noted that the Patent Office acknowledges that "the prior art does not specifically recite the concentration of protein in the sample as claimed." [Office Action, page 6] However, the Patent Office asserts that "such a limitation is merely an intended use which the prior art would inherently be capable of doing." [Office Action, page 6] According to M.P.E.P. § 2112, "[t]he fact that a certain result or

characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." [(citations omitted, emphasis in original)] More particularly,

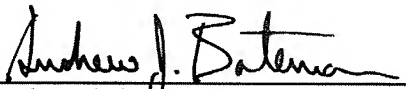
> [t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [M.P.E.P. § 2112 (citations omitted)]

"In relying upon the theory of inherency, the examiner *must* provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." [M.P.E.P. § 2112 (emphasis added and in original)] Accordingly, Applicants respectfully traverse the assertion of inherency and request that the Patent Office cite a document in support of this determination so that the Applicants have a full and fair opportunity to respond to the combination of documents.

For at least the foregoing reasons, it is respectfully submitted that Ding does not anticipate the subject matter of claims 1, 2, 5-7, 9, 10, 12, 69, and 70, and that Ding and Lee, whether considered alone or in combination, do not render the subject matter of claims 1, 2, 5-7, 9, 10, 12, 69, and 70 obvious. Accordingly, reconsideration and withdrawal of these grounds of rejection are respectfully requested.

All of the rejections raised in the Office Action having been addressed, it is respectfully submitted that the present application is in condition for allowance and a notice to that effect is earnestly solicited. Should the Examiner have any questions regarding this response or the application in general, the Examiner is urged to contact the Applicants' attorney, Andrew J. Bateman, by telephone at (202) 625-3547. All correspondence should continue to be directed to the address given below.

Respectfully submitted,

By: 

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